DOCKET NO.: NIHB-2264 PATENT

Application No.: 10/722.000

Office Action Dated: August 7, 2009

This listing of claims will replace all prior versions, and listings, of claims in the application.

## Listing of Claims:

1. (currently amended) An infectious chimeric respiratory syncytial virus (RSV) comprising a major nucleocapsid (N) protein, a nucleocapsid phosphoprotein (P), a large polymerase protein (L), a RSV M2 ORF1 RNA polymerase elongation factor (M2(ORF1)), and a partial or complete human RSV genome or antigenome of one RSV strain or subgroup combined with a heterologous gene or gene segment of a bovine or mouse RSV strain or subgroup virus to form a chimeric RSV genome or antigenome, wherein the chimeric genome or antigenome is further modified by one or more attenuating mutations selected from at least one and up to a full complement of attenuating mutations present within a panel of biologically derived mutant RSV strains, said panel consisting of cpts RSV 248 (ATCC VR 2450), epts RSV 248/404 (ATCC VR 2454), epts RSV 248/955 (ATCC VR 2453), epts RSV 530 (ATCC VR 2452), cpts RSV 530/1009 (ATCC VR2451), cpts RSV 530/1030 (ATCC VR 2455), RSV B-1 cp52/2B5 (ATCC VR 2542), and RSV B-1 cp-23 (ATCC VR 2579) the group consisting of Phe<sub>521</sub> Gln<sub>831</sub>, Met<sub>1169</sub> and Tyr<sub>1321</sub> of the L protein to another amino acid, or a nucleotide substitution of base T to C at position of 7605 in the gene-start sequence of gene M2.

## 2 - 3. (Canceled)

4. (original) The chimeric RSV of claim 1, wherein the heterologous gene or gene segment is selected from a NS 1, NS2, N, P, M, SH, M2(ORF1), M2(ORF2), L, F or G gene or gene segment.

## 5. - 17. (Canceled)

- 18. (previously presented) The chimeric RSV of claim 1, wherein the chimeric genome or antigenome incorporates at least two attenuating mutations.
- 19. (original) The chimeric RSV of claim 18, wherein the chimeric genome or antigenome incorporates attenuating mutations adopted from different biologically derived mutant RSV strains.

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20. (previously presented) The chimeric RSV of claim 1, wherein the chimeric

genome or antigenome includes at least one attenuating mutation stabilized by multiple

nucleotide changes in a codon specifying the mutation.

21. (Canceled)

22. (original) The chimeric RSV of claim 1 further comprising a nucleotide

modification specifying a phenotypic change selected from a change in growth

characteristics, attenuation, temperature-sensitivity, cold-adaptation, plaque size, host-range

restriction, or a change in immunogenicity.

23. (original) The chimeric RSV of claim 22, wherein a SH, NS1, NS2,

M2ORF2, or G gene is modified.

24. (original) The chimeric RSV of claim 23, wherein the SH, NS1, NS2,

M2ORF2, or G gene is deleted in whole or in part or expression of the gene is ablated by

introduction of one or more stop codons in an open reading frame of the gene.

25. - 27. (Canceled)

28. (original) The chimeric RSV of claim 22, wherein the nucleotide modification

comprises an insertion, deletion, substitution, or rearrangement of a translational start site

within the chimeric genome or antigenome.

29. - 34. (Canceled)

35. (original) The chimeric RSV of claim 1 which is a virus.

36. (original) The chimeric RSV of claim 1 which is a subviral particle.

37. (withdrawn) A method for stimulating the immune system of an individual to

induce protection against RSV which comprises administering to the individual an

immunologically sufficient amount of the chimeric RSV of claim 1 combined with a

physiologically acceptable carrier.

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38. (withdrawn) The method of claim 37, wherein the chimeric RSV is

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administered in a dose of 10<sup>3</sup> to 10<sup>6</sup> PFU.

39. (withdrawn) The method of claim 37, wherein the chimeric RSV is

administered to the upper respiratory tract.

40. (withdrawn) The method of claim 37, wherein the chimeric RSV is

administered by spray, droplet or aerosol.

41. (withdrawn) The method of claim 37, wherein the chimeric RSV is

administered to an individual seronegative for antibodies to RSV or possessing transplacentally

acquired maternal antibodies to RSV.

42. (withdrawn) The method of claim 37, wherein the chimeric RSV is a chimera

of human RSV A and RSV B which elicits an immune response against either human RSV A

or RSV B.

43. (withdrawn) The method of claim 37, wherein the chimeric RSV is a chimera

of human RSV A and RSV B which elicits an immune response against both human RSV A

and RSV B.

44. (withdrawn) The method of claim 37, wherein the chimeric RSV is a chimera

of human RSV A and RSV B which elicits an immune response against either human RSV A

or RSV B and is co-administered with an immunologically sufficient amount of a second

attenuated RSV capable of eliciting an immune response against human RSV A or RSV B,

whereby an immune response is elicited against both human RSV A or RSV B.

45. (withdrawn) The method of claim 44, wherein the chimeric RSV and second

attenuated RSV are administered simultaneously as a mixture.

46. (original) An immunogenic composition to elicit an immune response against

RSV comprising an immunologically sufficient amount of the chimeric RSV of claim 1 in a

physiologically acceptable carrier.

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47. (original) The immunogenic composition of claim 46, formulated in a dose of  $10^3$  to  $10^6$  PFU.

48. (original) The immunogenic composition of claim 46, formulated for administration to the upper respiratory tract by spray, droplet or aerosol.

## 49. - 63. (canceled)

- (withdrawn, currently amended) A method for producing an infectious 64. attenuated chimeric RSV particle from one or more isolated polynucleotide molecules encoding said RSV, comprising: expressing in a cell or cell-free lysate an expression vector comprising an isolated polynucleotide encoding a chimeric RSV genome or antigenome comprsing a partial or complete human RSV genome or antigenome of one RSV strain or subgroup virus combined with a heterologous gene or gene segment of a different bovine or mouse RSV strain or subgroup virus and RSV N, P, L and RNA polymerase elongation factor proteins, wherein the chimeric genome or antigenome is further modified by one or more attenuating mutations selected from at least one and up to a full complement of attenuating mutations present within a panel of biologically derived mutant RSV strains, said panel consisting of cots RSV 248 (ATCC VR 2450), cots RSV 248/404 (ATCC VR 2454), cots RSV 248/955 (ATCC VR 2453), epts RSV 530 (ATCC VR 2452), epts RSV 530/1009 (ATCC VR2451), epts RSV 530/1030 (ATCC VR 2455), RSV B-1 ep52/2B5 (ATCC VR 2542), and RSV B-1 ep-23 (ATCC VR 2579) the group consisting of Phes21 Gln831, Met 1169 and Tyr<sub>1321</sub> of the L protein to another amino acid, or a nucleotide substitution of base T to C at position of 7605 in the gene-start sequence of gene M2.
- 65. (withdrawn) The method of claim 64, wherein the polynucleotide encoding the chimeric RSV genome or antigenome and the N, P, L and RNA polymerase elongation factor proteins are expressed by two or more different expression vectors.